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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,574	02/01/2007	Jeffrey T. Borenstein	61947(51588)	6443
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EXAMINER				
YEAGER, RAYMOND P				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/568,574

**Applicant(s)**

BORENSTEIN ET AL.

**Examiner**

Raymond P. Yeager

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 9-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 13-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 February 2009 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/06)  
Paper No(s)/Mail Date 04/24/2008; 06/28/2007; 12/04/2006; 03/15/2006
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1 to 24 are pending.

#### ***Election/Restriction***

Applicant's election of group I, claims 1 to 8 and 13 to 24 in the reply filed on 09/22/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9 to 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 09/22/2009.

#### ***Priority***

This application 10/568,574 (02/01/2007) is a US National Stage entry of PCT/US04/26848 (08/18/2004) per 35 USC 371 and claims benefit of US Provisional Application 60/495,973 (08/18/2003) per 35 USC 119e. The '973 application does not have a positive recitation of defined structures on the floor of the channel or lateral alignment of nanotopographic features noted in instant claims 2, 5, 15, or 21. The '973 application does not recite the all the cell types in instant claims 8 and 24. The '973 application does not recite a centrally positioned membrane as in instant claim 16. As such, claims 2, 5, 8, 15, 16, 21, and 24 are considered to have a priority date of 08/18/2004 and claims 1, 3 to 4, 6 to 7, 9 to 14, 17 to 20, and 22 to 23 are considered to have a priority date of 08/18/2003.

#### ***Objection – Claims***

Claim 8 is objected to because of the following informalities: A comma seems to be omitted from between cardiac cells and fibroblasts. Appropriate correction is required.

***Claim Rejections – 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- Claims 1 to 5 and 7 to 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al, 1991 (*J Cell Sci*, vol. 99:73-77; provided by applicant on the 03/15/2006 IDS).

Applicant claims a substrate with nanotopographic features arranged to organize cell types into subassemblies within micromachined surface structures in the walls and floors of the channels. The nanotopographic features are generated by a lithographic technique, facilitate adhesion of a cell type to a desired location on the substrate, and may align the cells laterally.

Clark et al, 1991 teaches a substrate with nanotopographic features (i.e. 100 to 400 nm) arranged to organize BHK cells (i.e. kidney cells) across the elongated gratings on the substrate (i.e. laterally) (abstract, and page 74, column 1, paragraphs 1 and 7; and page 74, column 2, paragraph 2) (limitations in instant claims 1, 3 to 5, and 8). The surface structures in the grating were produced by photolithography (page 73, column 2, paragraphs 2-3) (limitations in instant claims 2 and 7).

- Claims 1 to 8, 13, 15, 17, and 19 to 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Desai 2000 (*Medical Engineering & Physics*, vol. 22:595-606; provided by applicant on the 03/15/2006 IDS).

Applicant claims a substrate with nanotopographic features arranged to organize cell types into subassemblies within micromachined surface structures in the walls and floors of the channels. The nanotopographic features are generated by a lithographic

technique, facilitate adhesion of a cell type to a desired location on the substrate, and may align the cells laterally or in a grid. The claims also recite a tissue engineered system comprising the substrate, a semi-permeable membrane, and a fluid communication system.

Desai 2000 teaches micromachining nanoscale structures by photolithography on a substrate to make pores and channels with nanometer scale morphology (i.e. architecture, topography, or features) is well known to one of ordinary skill in the art (page 596, column 1, paragraph 3) and further, Desai 2000 teaches topography provides control over cell growth and development in cells such as myocytes or fibroblasts (pages 596-597, section 2) (limitations in instant claims 1 to 4 and 7 to 8). Desai 2000 recites the cells may spread and migrate across an axis of lines (i.e. laterally) or in a grid (pages 596-597, section 2 and page 598, figure 6) (limitations in instant claims 5 and 6). Desai 2000 teaches tissue engineering systems as noted above and with a semi-permeable membrane layer microfabricated to contain nanostructures as small as 20 nm (pages 600-601, section 5) (limitations in instant claims 13, 15, and 19 to 24). Desai 2000 also recites combining microfluidic and laminar flow methods (i.e. which require pumping as a means for circulating fluid) with tissue engineering of a microfabricated scaffold (page 599, column 1, paragraph 5 to column 2, paragraph 1) (limitations in instant claim 17).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 to 8 and 13 to 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai 2000, as in claims 1 to 8, 13, 15, 17, and 19 to 24 above, in view of Borenstein et al, 2002 (*Biomedical Devices*, vol. 4(3):167-175; provided by

applicant on the 06/28/2007 IDS) and US Patent 5,665,596 (Publication date: 09/09/1997), hereafter referred to as the '596 patent.

Applicant claims a substrate with nanotopographic features arranged to organize cell types into subassemblies within micromachined surface structures in the walls and floors of the channels. The nanotopographic features are generated by a lithographic technique, facilitate adhesion of a cell type to a desired location on the substrate, and may align the cells laterally or in a grid. The claims also recite a tissue engineered system comprising the substrate, a semi-permeable membrane, and a fluid communication system. The fluid communication system provide nutrients and removes waste. The semi-permeable membrane may be between layers or centrally dividing a compartment to provide for a different cell type on each side.

As discussed *supra*, Desai 2000 teaches a microfluidic tissue engineering system comprising a substrate with nanoscale structures formed by lithography to provide control over cell growth with a semi-permeable membrane layer microfabricated to contain nanostructures (limitations in instant claims 1 to 8, 13, 15, 17, and 19 to 24).

Desai 2000 differs from the instant application in that it does not expressly teach providing a semi-permeable membrane between layers or in a central compartment with separate cell types on each side of the membrane or a nutrient supply and waste removal in fluid communication with the system. This deficiency in Desai 2000 is cured by the teachings of Borenstein et al, 2002 and the '596 patent. Borenstein et al, 2002 teaches that the fluid communication provides the media (i.e. nutrients) (page 167, column 2, paragraph 2; and page 173, figure 10) and would necessarily carry away waste products (limitations in claims 17 and 18). The '596 patent teaches providing a centrally positioned semi-permeable membrane to separate the chamber into two parts with a different cell type on each side ('596, abstract, and columns 2-3) (limitations in instant claims 14 and 16). Note that it would also be obvious to provide the semi-permeable membrane between layers (Borenstein et al, 2002, page 171, column 1, paragraph 1) as this semi-permeable membrane would separate the canal into two compartments, as taught by the '596 patent.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide a tissue engineering system comprising a substrate with nanoscale structures for the organization of cell types with a semi-permeable membrane with a flow of fluids as taught by Desai 2000 provide fluid communication for the transport of nutrients and metabolites as taught by Borenstein et al, 2002, and provide a semi-permeable membrane at the center of a canal as taught by the '596 patent. One of ordinary skill in the art would have been motivated to do this because Borenstein et al, 2002 teaches the vascular supply is required in tissue engineering to provide nutrient and metabolite transport (page 167, column 2, paragraph 2) and the '596 patent teaches this method of co-culture provides a method to study inflammation and cell differentiation ('596, column 1, lines 11-24). In light of the forgoing discussion, it would be obvious to one of ordinary skill in the art that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

- Claims 1 to 4, 8, 13 to 18, and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 118, 124 to 126, 130, 134 to 139, 141, 235, 272, 282, and 288 to 290 of copending Application No. 10/187,247, hereafter referred to as the '247 application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '247 patent is considered a species which anticipates the instant claim set.

The instant claims recite a tissue engineering system comprising a substrate with nanoscale structures for the organization of cell types with a semi-permeable membrane, and a fluid communication system for nutrient and metabolite transport. The semi-permeable membrane may be between layers or centrally dividing a compartment. As the instant claims recite both nanotopographic features and micromachined surface features the surface morphology is considered to comprise microstructures and/or nanostructures (limitations in instant claims 1 to 4, 8, 13 to 18, and 24).

The '247 application teaches a tissue lamina (i.e. engineered tissue) comprising multiple layers with a first polymeric scaffold with microchannels and animal cells, a second polymeric scaffold with animal cells, and a semi-permeable membrane in between the polymeric scaffolds in a fluid communication system ('247, claim 118). The



recitation "for the circulating fluid" is considered an intended use for the semi-permeable membrane and the microchannels; the instant claims are considered to have the same properties ('247, claims 118, 124 to 126, 130, 134 to 139, 141, 235, 272, 282, and 288 to 290).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

- Claims 13 to 14, 16 to 18 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 to 2, 6, 24, 32 to 36 of copending Application No. 10/557,081, hereafter referred to as the '081 application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope.

The instant claims recite a tissue engineering system comprising a substrate with nanoscale structures for the organization of cell types with a semi-permeable membrane, and a fluid communication system for nutrient and metabolite transport. The semi-permeable membrane may be between layers or centrally dividing a compartment. (limitations in instant claims 13 to 14, 16 to 18 and 24).

The '081 application teaches a three-dimensional system comprising at least two layers with a centrally positioned membrane separating each compartment wherein each compartment comprises different cell types and a fluid communication system ('081, claims 1 to 2, 6, 24, 32 to 36).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

- Claims 13 to 19, and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 13, 19, 20, and 34 to 36 of copending Application No. 12/058,128, hereafter referred to as the '128 application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope.

The instant claims recite a tissue engineering system comprising a substrate with nanoscale structures for the organization of cell types with a semi-permeable membrane, and a fluid communication system for nutrient and metabolite transport. The semi-permeable membrane may be between layers or centrally dividing a compartment. As the instant claims recite both nanotopographic features and micromachined surface features the surface morphology is considered to comprise microstructures and/or nanostructures (limitations in instant claims 13 to 19, and 24).

The '128 application teaches a multilayer device comprising a first layer with microchannels and suitable for cell attachment and a second layer suitable for cell attachment and a fluid communication system ('128, claims 1, 3, 13, 19, 20, and 34 to 36).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Due to the large number of double patenting rejections, applicant is reminded that "the individuals covered by 37 CFR 1.56 have a duty to bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications which are 'material to patentability' of the application in question" (see MPEP § 2001.06(b) and MPEP 2004, paragraph 9).

***Conclusion***

No claims are allowed; all claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond P. Yeager whose telephone number is (571) 270-7681. The examiner can normally be reached on Mon - Thurs 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

R.P.Y.

/Leon B Lankford/

Primary Examiner, Art Unit 1651